REMARKS/ARGUMENTS

As requested by the Office, the Applicants have attached pages 3-8 of IDS Form 1449. The Applicants have also attached a Supplemental IDS that references a related case specifically, serial number 10/258,493 which is a 35 U.S.C. section 1.371 national case which is equivalent to the PCT international application number US01/12983. The Examiner is urged to review these two documents, i.e., PCT serial number US01/12983 and U.S. serial number 10/258,493 and the prosecution thereof.

Claims 7, 31, 32, 35-38, 40, 41, 94, 95, 101, 115-122 and 124-131 are pending in the present Application.

Claims 1-6, 8-30, 33-34, 39, 42-93, 96-100, 102-104, and 123 were previously canceled. Claims 7, 31-32, 36-38, 40-41, 95, 101, 115-122, 124-129, 130-131 were previously presented. Previously withdrawn Claims 132-137 have been canceled in this response. Claims 35 and 94 are Original Claims.

I. Information Disclosure Statement

As requested, Applicants have enclosed sheets 3-8 of Form 1449 of the Information Disclosures Statement so that the Examiner may initial the listed references to indicate that they have been considered.

II. Impermissible Hindsight

The Office has rejected Claims 7, 31, 32, 35-38, 40, 41, 94, 95, 101, 115-122, and 124-131 under 35 U.S.C. 103(a) as being unpatentable over Merck WO 94/26731, alone, in view of Ando et al, US Patent 6,294,558, Haruta et al, US Patent 6,362,209 and Kimura et al, EP799,823.

The Office states that the Merck reference discloses a genus of 3-(4-methylsulfonylphenyl or 4-sulfamoyl-phenyl) 4-aryl or hetaryl-thiophenes where the 4-methylsulfonylphenyl and the 4-sulfamoylphenyl groups may be substituted in the 3-position with a halogen selected from fluoro, chloro, bromo or iodine, carboxy or CF3 as COX-2 inhibitors. The Office then states that when fluoro is selected, the instant compounds are covered. The Office states that **if** it could be shown that the later art recognized the particular efficacy of this type of fluoro

substitution in this group of CoX-2 inhibitors, then the making of the instant 3-(3-fluoro-4-methylsulfonylphenyl) or 3-(3-fluoro-4-sulfamoylphenyl) 4-aryl or hetaryl thiophenes as COX-2 inhibitors **would have been motivated** and the instant compounds obvious.

Similarly, the Office states that Ando et al shows this for similar compounds differing from the instant compounds in that the 4-aryl moiety is substituted in the 4-position by an aryl group. By the Office's own admission, the Office states that "**a wide variation for the central aromatic nucleus which is denoted as A therein**" exists, and that A can be the instant thienyl "**as well as many other hetaryl moieties** including pyrrolyl and oxazolyl" (emphasis added). The Office alleges that if one skilled in the art **knew** that the 3-fluoro-4-methylsulfonyl or 3-fluoro-4-sulfamoyl substitution were preferred in this class of COX-2 inhibitors not containing the 4-position aryl substitution on the other aryl substituent then the selection of 3-fluoro-4-methylsulfonyl or 3-fluoro-4-sulfamoyl substitution **would have been obvious.**

The Office asserts states that this is also shown by the Haruta et al reference for compounds where the central hetaryl moiety is oxazole rather than the instant thienyl group

Lastly, the Office alleges that this is also shown in the Kimura et al reference, for pyrroles of the formulae of Examples 1-161 to 1-166 in Table 1, and Examples 2-152 to 2-160 in Table 2 for the 3-position for fluoro.

The Office thus rationalizes that the instant class of 3-(3-F-4-methylsulfonylphenyl or 3-F-4-sulfamoylphenyl)-4-aryl thiophenes as COX-2 inhibitors would have been obvious to one of ordinary skill in the art.

However, the Applicants contend that out of the galaxy of compounds that could be formed from the formulae defined in each of these references, nothing in these references would lead one to those compounds in the present invention. Thousands of compounds can be made from the formulas listed in these three references, yet only hindsight reconstruction would lead the skilled artisan to the compounds of the present invention.

Further, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient to establish a prima-facie case of obviousness. There still must exist some motivation or suggestion to make the claimed invention.

In each of the cited references previously discussed, there is no motivation to select the compounds of the present invention coupled with the fact that in any one of these references, the variables of the formulae are so numerous that the number of different possible combinations of variables totals potentially thousands of different compounds. Nowhere do the disclosures of these cited references suggest that one should select the precise variables of the present invention from the potentially thousand possible combinations.

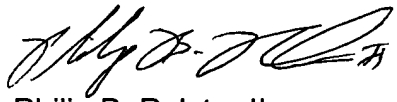
The Office is applying "hindsight reconstruction" by using the teaching of the Applicant's patent application as a guide for searching and analyzing the reference in the right way to arrive at the Claims at issue. Such hindsight reconstruction is improper in a rejection under U.S.C. § 103.

In view of the foregoing, Applicants respectfully request that the rejection of Claims 7, 31, 32, 35-38, 40, 41, 94, 95, 101, 115-122, and 124-131 under 103 be withdrawn and the claims be examined on their merits and allowed.

III. Conclusion

If the Examiner believes a telephonic interview with Applicant's representative would aid in the prosecution of this application, the Examiner is cordially invited to contact Applicant's representative at the below listed number.

Respectfully submitted,



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